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META-ANALYSIS OF THE ASSOCIATION BETWEEN A COMMON VARIANT IN THE BETA-2 ADRENERGIC RECEPTOR AND SUDDEN CARDIAC DEATH

ACC Poster Contributions
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Background: Homozygosity of a common non-synonymous single nucleotide polymorphism (SNP) in the Beta-2 Adrenergic Receptor gene (ADRB2) that results in substitution of glutamine for glutamic acid at position 27 (Gln27Glu) has been inconsistently associated with an increased risk of sudden cardiac death (SCD). These discrepant results could be due to small sample sizes of individual studies, and no combined meta-analysis has been performed.

Methods and Results: We conducted a two part meta-analysis. First, to increase sample size, we determined genotypes for the Gln27Glu variant in 492 cases of sudden cardiac death and 1388 controls drawn from individuals of European ancestry enrolled in six prospective cohort studies. Cases were matched to controls on age, sex, cohort, history of CVD at the time of blood draw, and follow-up time. Conditional logistic regression with fixed effects meta-analysis assuming a recessive model, as previously reported in the literature, was used to test for association. When these six individual study results were combined in meta-analysis, homozygosity for the Gln27 allele conferred a non-significant increase in the age-adjusted odds ratio (OR) for SCD of 1.22 (95% CI: 0.98-1.53; P=0.08). After controlling for age, history of diabetes, hypertension, and high cholesterol, smoking status, body mass index, physical activity, aspirin use, alcohol intake, and parental history of early myocardial infarction, the association was statistically significant (OR=1.30, 95% CI: 1.01 to 1.67; P=0.046). When combined with two previous reports in an additional meta-analysis, there was a significant association between ADRB2 genotype and SCD (OR=1.31, 95% CI: 1.10-1.56; P=0.003).

Conclusions: Homozygosity for the Gln27 allele in ADRB2 is associated with a 30% increased risk of SCD in this combined meta-analysis of 730 cases of SCD in population based studies.